REMARKS

New Claims 30-36 have been added. As a result, Claims 11 and 19-36 remain pending in the present application. Support for the amendments is found in the specification and claims as filed. Accordingly, the amendments do not constitute the addition of new matter. Reconsideration of the application in view of the foregoing amendments and following comments is respectfully requested.

Rejection under 35 U.S.C. § 103

The Examiner rejected Claims 11 and 20-25 under 35 U.S.C. § 103(a) as being anticipated by Mizutani et al. in view of Caspar et al. and further in view of CN1127070.

In the Office Action, the Examiner stated that it was "implicit" in the teaching of Mizutani to identify human individuals with osteoporosis. The Examiner also implied that the cited references inherently teach the treatment of "bone loss" as a result of osteoporosis. However, the invention of Claims 11 and 20-25 is not directed to osteoporosis in general, nor is it directed to "bone loss." Rather, these claims are directed to "[a] method for increasing bone breaking load and strength in a mammal." As discussed below, this is quite distinct from the treatment of osteoporosis in general or of bone loss in particular.

Osteoporosis can be caused by a number of factors. There are two types of bone regulating cells. The osteoclasts function to dissolve older bone and leave tiny unfilled spaces behind; the osteoblasts then move into these spaces to produce new bone. The process of dissolving older bone mass by osteoclasts and new bone formation by osteoblasts is the mechanism for the repair and continuing strength of bone. (See website: http://www.lef.org/magazine/mag99/mar99-report1.html on 9/26/05.)

Osteoporosis can result from a number of pathophysiological mechanisms. Multiple factors cause the net loss of bone mass seen in persons with osteoporosis including too many bone remodeling units (osteoclasts), which results in an imbalance of osteoclasts and osteoblasts at the resorption site. Depletion or too few osteoblasts can also lead to osteoporosis because the remodeled site is not properly filled with osteoblast cells during the bone remodeling process. (See website: http://www.medscape.com/viewarticle/450674_2 on 9/26/05.) Accordingly, there

are a number of pathophysiological mechanisms that can cause this one disease, osteoporosis. Therefore, when identifying individuals at risk for osteoporosis is considered, the different pathophysiological mechanisms can serve as identifying factors. Claims 11 and 20-22 identify mammals for treatment based on one of these factors. To reject Claims 11 and 20-25 under 35 U.S.C. § 103(a), the cited references must teach or suggest the identification of patients based on the same pathophysiological criteria recited in Claim 11.

None of the cited prior art references disclose or suggest a method involving patients in need of increased breaking load and strength, as recited in Claim 11. Mizutani et al. discloses only that resveratrol directly stimulates cell proliferation and differentiation of osteoblasts *in vitro*. Mizutani et al. discloses nothing regarding the effect of resveratrol on increased breaking load strength. The Examiner appears to imply that such a disclosure is inherent in Mizutani. However, according to M.P.E.P. 2112, "[t]o establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." As discussed below, increased bone breaking load and strength are not a necessary result of the increased osteoblast activity disclosed by Mizutani.

Example 1 on pages 34-35 of the Applicants' specification shows that the breaking load and breaking energy are not correlated with bone density. In fact, even though bone density is decreased, when the resveratrol group is compared to the sham group, the breaking loads and breaking energy are increased. The disclosure in Mizutani et al. of stimulating cell proliferation and differentiation of osteoblasts would suggest that bone density would be increased because osteoblasts are responsible for producing new bone in unfilled spaces. Thus it is entirely unexpected in view of Mizutani that breaking load and breaking energy would be increased. Caspar et al. on page 19 also discloses the use of resveratrol for osteogenic cell differentiation and mineralized bone formation. Thus, like Mizutani et al., Caspar et al. gives no disclosure or suggestion of increasing bone breaking load and energy. CN 1127070 discloses a milk powder without disclosure or suggestion of the use of a stilbene-like compound for strengthening formed bone. Accordingly, the combination of references fails to suggest the invention of Claim 11.

Without a showing of increasing breaking load and breaking energy in bones of a mammal, the cited references lack the descriptive matter necessary for an obviousness rejection of the presently pending Claims 11 and 20-25. There is no inherent or explicit showing in the cited references that the recited mechanism is present. Accordingly, the cited references do not teach or suggest the claimed invention.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw these rejections under 35 U.S.C. § 103(a).

New claims

New Claims 30-36 have been and are directed to "a method for preventing or treating any of menopausal or postmenopausal diseases accompanied by a decrease in bone weight in a mammal comprising suppressing lowering bone density in said mammal."

As shown below, one embodiment, resveratrol, has an effect of suppressing lowering bone density in a patient with menopausal or postmenopausal diseases. The effect is shown in Experimental Example 1, especially Table 1, of the specification, as evidenced by the enclosed article by Ezawa (*J. Jpn. Soc. Nutr. Food Sci.*, Vol. 49, 247-257 (1996)) with a partial English language translation.

Chapter 3 of Ezawa discloses that calcium content of the femur in the rats without ovary (OVX group) was significantly lower than that of rats with ovary (Sham group). Since Ca content in a bone correlates closely with bone density, Ezawa teaches that ovariectomizing causes decrease of bone density. Experimental Example 1, by contrast, discloses that there is no significant difference in the bone density of between the rats without ovaries fed with food containing resveratrol (resveratrol group) and that of sham group.

Ezawa teaches that ovariectomizing causes significant decrease of bone density, nonetheless, ovariectomizing rats that were fed resveratrol did not show significant decrease of bone density in Experimental Example 1. Accordingly, Claims 30-36 directed to "a method for preventing or treating any of menopausal or postmenopausal diseases accompanied by a decrease in bone weight in a mammal comprising suppressing lowering bone density in said mammal" are

supported by the data in the specification teaching that resveratrol can suppress decrease of bone density caused by ovariectomizing.

Moreover, Claims 30-36 are patentable over the cited prior art of record in the Office Action mailed November 24, 2004. The Examiner relied on Mizutani et al. to show that resveratrol directly stimulates cell proliferation and differentiation of osteoblasts *in vitro*. Similarly, the Casper reference discloses the use of resveratrol for osteogenic cell differentiation and mineralized bone formation. CN 1127070 discloses a laundry list of ingredients for a composition and asserts numerous conditions that can be treated with administration of the composition.

While Claims 30-36 are directed to "a method for preventing or treating any of menopausal or postmenopausal diseases accompanied by a decrease in bone weight in a mammal comprising suppressing lowering bone density in said mammal," the prior art teaches that bone formation is a result of a direct stimulatory effect on bone formation. Accordingly, the cited prior art do not show that resveratrol can suppress decrease of bone density caused by ovariectomizing by suppressing lowering bone density in a mammal. As such, Claims 30-36 are patentable over the cited prior art.

CONCLUSION

In view of the foregoing amendments and comments, it is respectfully submitted that the present application is fully in condition for allowance, and such action is earnestly solicited.

The undersigned has made a good faith effort to respond to all of the rejections in the case and to place the claims in condition for immediate allowance. Nevertheless, if any undeveloped

issues remain or if any issues require clarification, the Examiner is respectfully invited to call the undersigned in order to resolve such issue promptly.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: September 27, 2005

By: _____

Connie C. Tong
Registration No. 52,292
Agent of Record
Customer No. 20,995
(949) 760-0404

1948609
092205